



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION,
PESTICIDES
AND TOXIC
SUBSTANCES

December 14, 2010

MEMORANDUM

Subject: Efficacy Review for EPA Reg. No. 84020-1, BluTab Waterline
Maintenance Tablets; DP Barcode: 383880

From: Tajah Blackburn, Ph.D., Microbiologist
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Product Science Branch
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[Signature]
12/14/10

To: Marshall Swindell PM 33/ Zebora Johnson
Regulatory Management Branch I
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Applicant: ConFirm Monitoring System, Inc.
109 Inverness Drive East Unit F
Englewood, CO 80112-5105

Formulation from the Label:

<u>Active Ingredient(s)</u>	<u>% by wt.</u>
Silver.....	0.477%
<u>Other Ingredients</u>	<u>99.523%</u>
Total.....	100.000 %

I BACKGROUND

The product, BluTab Waterline Maintenance Tablets (EPA Reg. No. 84020-1) is a registered product. According to the registrant's representative's letter, BluTab Waterline Maintenance Tablets are designed to clean and prevent the growth of bacteria on a continual basis in dental unit water lines. The current submission is to request "traditional...non-public health claims by the EPA". The claims the registrant is "seeking are the same, similar to, those granted to Citrisil, EPA Reg. No. 83315-1." To support the proposed additional non-public health label claim of "maintains ≤ 10 cfu/ml in dental unit water line effluent", the registrant submitted efficacy data generated at the Baylor College of Dentistry at Texas A&M University Health Science Center (Dallas, TX). Study was not conducted under Good Laboratory Practices (40 CFR 160).

The current data package contained a letter from the registrant's representative (SRC Consultants, dated September 28, 2010), Statement of No Data Confidentiality, one efficacy study (MRID No. 482480-01), and the proposed label.

II USE DIRECTIONS

The product is designed to clean and prevent the growth of bacteria on a continual basis in dental unit water line systems. Directions on the proposed label provided the following directions for the preparation and use of the product:

Initial Treatment

Before starting a treatment program, flush lines with a waterline cleaner or another product recommended by the equipment manufacturer to remove line buildup or deposits. When flushing dental unit waterlines, always follow a recognized line flushing/cleaning protocol. Repeat flushing to clean lines every 2 month or more frequently when water quality result indicate.

Routine Treatment (Directions for 419 mg tablets)

- (1) Place tablet or tablets in empty dental unit water bottle every time you refill the water. This product is intended for use with potable water (including tap or distilled).
- (2) Fill bottle with desired volume of water and connect to dental unit. Tablet dissolves in a few minutes.

Water Volume	Tablets
2L (68 fl. oz.)	1
4L (135 fl. oz.)	2

- (3) This product may be left in the waterlines overnight and for extended periods of non-use. Use water solution until it is expended or up to 28 days. It is not necessary to purge lines at the end of each day.

Routine Treatment (Directions for 146 mg tablets)

- (1) Place tablet or tablets in empty dental unit water bottle every time you refill the water. This product is intended for use with potable water (including tap or distilled).
- (2) Fill bottle with desired volume of water and connect to dental unit. Tablet dissolves in a few minutes.

Water Volume	Tablets
700-750 (24-25 fl. oz.)	1
1500 (51 fl. oz.)	2
2000 (68 fl. oz.)	3

- (3) This product may be left in the waterlines overnight and for extended periods of non-use. Use water solution until it is expended or up to 28 days. It is not necessary to purge lines at the end of each day.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

No standard exist for the proposed claims.

IV SYNOPSIS OF SUBMITTED EFFCACY STUDY

1. MRID No. 482480-01, "Efficacy of a Silver Dental Line Treatment" for BluTab Waterline Maintenance Tablets by Dr. Raghunath Puttaiah and Mr. Shih-Ming Lin. Study Completion Date—February 26, 2007. Laboratory Project Number—76640.

The product was removed from their respective foil pouches on a daily basis or as needed. One tablet was added to each self-contained reservoir (750 ml PTFE bottle) with 700 ml of municipal or deionized water. The tablet dissolved in 1 minute. Dissolution, the self-contained reservoir was reattached to the DUWL Simulation device. The bottled were only refilled with water and another tablet when they became empty. DUWL from operating dental units (10 years or older) were harvested and attached to the Automated Dental Unit Water System Simulator. The Simulator was run with municipal water for about 1 month to maintain biofilms and heterotrophic contamination. The municipal water pH was approximately 7.0-7.5 and the total dissolved solids concentration was approximately 180 ppm and 250 ppm. Line samples were removed from each unit to evaluate the biofilm baseline using Scanning Laser Confocal Microscopy. Before study initiation, water samples were collected from each unit to measure the level of bacteria using a heterotrophic plate count (HPC). HPC demonstrated contamination of >600,000 CFU/ml from the collected water in each dental unit. The Automated DUWL System Simulator was controlled by an air solenoid, which in turn was manipulated by a logic controller. Water usage was calibrated manually to use up to 650 ml/6 hour work day and a randomized cumulative time of 12 minutes per

hour. Three units with self-contained reservoirs for irrigation were used in the study. Briefly:

Unit 1 (Treatment Unit 1): This dental unit was cleaned with chlorine dioxide initially to remove the existing biofilm in the lines. The lines were treated to three 10-minute contents with 50-600 ppm chlorine dioxide (Aseptrol), and then flushed with 500 ml of the BluTab 1 ppm solution (1 tablet in 700 ml municipal water). For the 12 week study period, 700 ml municipal water mixed with one BluTab was used for irrigation.

Unit 2 (Control Unit): This dental unit was cleaned with chlorine dioxide initially to remove the existing biofilm as described above for Unit 1. Following treatment, the lines were flushed with deionized water. For the 12 week study period, this unit was irrigated with deionized water.

Unit 3 (Treatment Unit 2): This dental unit did not undergo any initial cleaning with chlorine dioxide. For the 12 week study period, 700 ml municipal water mixed with one BluTab was used for irrigation.

Baseline and weekly water samples were collected in sterile containers. The lines hold approximately 20 ml water, so 10 ml water was collected before use in the morning. These were pooled samples (4 hand piece and 1 Air/Water Syringe lines from each simulation unit) of about 2 ml each. All the external effluent areas (6 inches) of the tubing were cleaned with an alcohol swab twice before collected to control external contamination. The collected water was neutralized with sodium thiosulfate by mixing 0.1 ml water sample in 0.9 ml sodium thiosulphate and holding for 30 seconds. A 1.0 ml aliquot of the neutralized sample was plated on R2A agar, incubated at room temperature (22°C) for 7 days and the survivors counted. Water samples were plated in triplicate. Sterility controls were conducted in parallel. The deionized source water was also plated with the study samples.

Line samples were collected at baseline and at the conclusion of the 12 week study. The end of the line closer to the hand piece/air-water syringe was sampled for this study as it is the most distal to the self-contained water system. The area of the waterline to be harvested was wiped with an alcohol swab on the outside and handled aseptically. The blade used to slice the line was wiped clean with an alcohol swab. A 1 cm section of line from each Unit was removed, slit axially and immediately dyed using the BacLight Green and Red Stain. While being observed using confocal microscopy, the sample holding mount/slide was wiped with an alcohol swab and sterile water was used for immersion. No neutralization of the biofilm samples was conducted. Following staining, the lines were immediately studied using Scanning Laser Confocal Microscopy. The biofilms were observed using an immersion lens at 400X and 1600X. The lines were quantitated evaluated for presence of a mature biofilm matrix, clumps of cells with no mature matrix, individually scattered cells, and line surfaces with no cells.

V RESULTS

Bacterial Levels of Effluent Water Samples in CFU/ml

Week	Samples	DI Source Water	Effluent		
			Test	Test	Control
			Unit 1	Unit 2	Unit 3
Baseline	1	0	>6,000	>6,000	>6,000
	2	0	>6,000	>6,000	>6,000
	3	0	>6,000	>6,000	>6,000
	Mean	<10	>6,000	>6,000	>6,000
1	1	0	0	0	0
	2	0	0	0	0
	3	0	0	0	0
	Mean	<10	<10	<10	<10
2	1	0	0	0	460
	2	0	0	0	210
	3	0	0	0	260
	Mean	<10	<10	<10	310
3	1	0	0	0	1200
	2	10	0	0	440
	3	30	0	0	1240
	Mean	20	<10	<10	960
4	1	0	0	0	790
	2	0	0	0	3290
	3	0	0	0	4020
	Mean	<10	<10	<10	2700
5	1	20	0	0	>6,000
	2	0	0	0	>6,000
	3	30	0	0	>6,000
	Mean	20	<10	<10	>6,000
6	1	0	0	0	>6,000
	2	0	0	0	>6,000
	3	0	0	0	>6,000
	Mean	<10	<10	<10	>6,000
7	1	0	0	0	>6,000
	2	0	0	0	>6,000
	3	0	0	0	>6,000
	Mean	<10	<10	<10	>6,000
8	1	0	0	0	>6,000
	2	0	0	0	>6,000
	3	0	0	0	>6,000
	Mean	<10	<10	<10	>6,000
9	1	30	0	0	>6,000
	2	80	0	0	>6,000
	3	70	0	0	>6,000
	Mean	60	<10	<10	>6,000
10	1	0	0	0	>6,000
	2	0	0	0	>6,000
	3	0	0	0	>6,000
	Mean	<10	<10	<10	>6,000
11	1	0	0	0	>6,000
	2	0	0	0	>6,000
	3	0	0	0	>6,000
	Mean	<10	<10	<10	>6,000
12	1	0	0	0	>6,000
	2	60	0	0	>6,000
	3	0	0	0	>6,000
	Mean	20	<10	<10	>6,000

According to the results provided in the test summary, the following findings were observed:

- (1) Upon initiation of the study, all units had mature biofilms and heterotrophic bacterial counts in excess of 600,000 CFU/ml
- (2) The deionized source water had mean microbial counts that ranged from <10 CFU/ml to 80 CFU/ml.
- (3) Unit 1 was initially cleaned with a high concentration of chlorine dioxide and used a continuous treatment of BluTab as a dental line irrigant reduced and maintained microbial counts at less than 10 CFU/ml for 12 weeks and showed visual confocal micrographs settlement of only a few cells on the line surface over the 12 week study.
- (4) Unit 2 (Control unit) was initially cleaned with a high concentration of active chlorine dioxide and used deionized water (low pH and low total dissolved solids) showed initial reduction in microbial counts due to chlorine dioxide cleaning. However, within 5 weeks the effluent became extremely contaminated, exceeding 6,000 CFU/ml. This line exceeded CDC/ADA guidelines by week 3. In addition, there was confocal microscopy evidence in the line.
- (5) Unit 3 had mature biofilms, was not cleaned with chlorine dioxide and only used a continuous treatment of a silver ion antimicrobial agent in municipal water as a dental line irrigant showed control of planktonic microorganisms in spite of the presence of a mature biofilm. BluTab was effective in keeping the bacterial counts in the effluent water at < 10 CFU/ml throughout the 12 weeks.

VI CONCLUSIONS/RECOMMENDATIONS

1. The Agency lacks both a test protocol and performance standard to support control of microbial contamination in dental unit waterlines. To support these claims, the Agency will rely upon field data to support the following non-public health claims, consistent with past registrations:

- (a) Dental Unit Waterline Treatment
- (b) For the Cleaning and Control of Microbial Contamination in Dental Unit Waterline
- (c) Inhibits the Growth of Microbial Contamination in Dental Unit Waterline
- (d) Maintains dental water line effluent ≤ 10 cfu/ml
- (e) Keeps Microbial Contamination in Dental Unit Water Lines in [Check] [Control]
- (f) Reduces and Maintains the Level in Microbial Contamination in Dental Unit Waterlines
- (g) Maintains ≤ 10 cfu/ml in dental unit waterline effluent